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10/630,170	07/30/2003	Sekhar Boddupalli	0118-CIP	7649
76656	7590	09/22/2009		
Patent Docket Department Armstrong Teasdale LLP One Metropolitan Square Suite 2600 St. Louis, MO 63102-2740				
EXAMINER				
SCHLIENTZ, LEAH H				
ART UNIT		PAPER NUMBER		
1618				
NOTIFICATION DATE		DELIVERY MODE		
09/22/2009		ELECTRONIC		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

USpatents@armstrongteasdale.com

### Office Action Summary

**Application No.**

10/630,170

**Applicant(s)**

BODDUPALLI ET AL.

**Examiner**

Leah Schlientz

**Art Unit**

1618

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 03 June 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-10 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-10 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

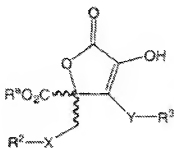
- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SF/ICE)  
Paper No(s)/Mail Date See Continuation Sheet
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☒ Other: Renumbered claims

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :3/7/2005, 12/18/2003, 11/25/2003.

## DETAILED ACTION

### *Election/Restrictions*

Applicant's election of dermatitis as condition, and the following compound in the reply filed on 6/3/2009 is acknowledged:



where X and Y = S, R<sup>1</sup> = COOR, R is H or alkyl, R<sup>2</sup> and R<sup>3</sup> can be the same or different and are preferably selected from optionally substituted aryl, optionally substituted heteroaryl, optionally substituted heterocyclic, and optionally substituted benzylic. Example compounds of 99-100 are said to exemplify the Markush above.

### *Priority*

It is noted that the instant Application is a continuation-in-part of US 10/354,474, filed 1/30/2003, now US 6,667,330, which claims benefit of US provisional 60/353,939. Upon examination of the '939 provisional application, support was not found for the instantly claimed method of treatment for a mammal suffering from a dermatologic condition comprising administering a therapeutically effective amount of a compound of formula I, including conditions such as dermatitis, etc. Accordingly, the effective filing

date of the instant claims is considered to be the filing date of the '330 Application, or 1/30/2003.

### ***Claim Objections***

The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims 7-9 have been renumbered 8-10.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for in vitro reduction of inflammation, does not reasonably provide enablement for treatment of a mammal suffering from any dermatologic condition. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

- 1) the quantity of experimentation necessary,
- 2) the amount of direction or guidance provided,
- 3) the presence or absence of working examples,
- 4) the nature of the invention,
- 5) the state of the prior art,
- 6) the relative skill of those in the art,
- 7) the predictability of the art, and
- 8) the breadth of the claims.

The instant specification fails to provide guidance that would allow the skilled artisan to practice the instant invention without resorting to undue experimentation, as discussed in the subsections set forth herein below.

*The nature of the invention and the state of the prior art*

The invention is drawn to a method of treating a mammal suffering from a dermatologic condition, dependent claims include conditions selected from regulating skin condition, regulating the skin aging, treating dermatitis, skin irritation, acne, rosacea, psoriasis, age-related damage, damage from UV radiation, environmental pollution, stress or fatigue, by administration of a compound of formula I or III. The art is well-developed with regard to treatments of certain dermatologic conditions using certain pharmaceutical formulations. For example, acne may be treated with benzoyl peroxide, warts may be treated with salicylic acid, ringworm may be treated with certain antifungals. However, the art is underdeveloped with regard to the teaching of a single class of compounds that are useful to treat any and all dermatologic conditions.

*The breadth of the claims, the relative skill of those in the art, and the predictability of the art*

The claims are very broad and are inclusive of methods of treating any dermatologic condition using a compound of formula I or III. There are millions of possible compounds encompassed by the claimed group of compounds having structural variables  $R^{1-4}$ , X and Y. There are a wide variety of dermatologic conditions encompassed by the instant claims which may have widely diverse etiology. Dermatologic conditions can include acne, albinism, athletes foot, birthmarks, boils, burns, cellulitis, cuts, dandruff, dermatitis, dry skin, eczema, folliculitis, herpes simplex, hives, lichen planus, melanoma, moles, rosacea, shingles, warts, wrinkles, etc., among others. Despite the advanced training of the ordinary practitioners in the pharmaceutical development and medical treatment arts, the arts are highly unpredictable. The state of the art is such that it is not possible to predict the activity of a compound, whether in vitro or in vivo, based on the structure alone. Typically, for the development of a method of treating a disease, a certain pharmacological property of a compound, such as receptor binding or activation, or cytotoxicity, must be tested or verified in an in vitro model. As stated, the state of the art is such that it is impossible to predict the in vitro activity of a compound based on the structure of a compound, even if a similar or structurally related compound has been shown to possess the desired in vitro activity. It is well recognized in the art that small modifications in a compound's structure can have profound effects on the compound's biological activity. Thus, the in vitro activity of a series of compounds must typically be verified individually. In order to

predict the *in vivo* activity of a compound based on the *in vitro* assay, the assay itself must be definitively well correlated to the pathophysiology of a target disease and verified as being predictive of the *in vivo* activity of a compound. For example, if a receptor is known to be overactivated in the pathophysiology of a disease, the ordinary practitioner would predict that a compound that inhibits the activation of the receptor may be useful for the treatment of said disease. However, even for *in vitro* models that involve receptors known to be involved in the pathophysiology of a disease, translating the *in vitro* efficacy of a compound to *in vivo* efficacy for the treatment of a disease is notoriously unpredictable unless the correlation has been conclusively verified. Further, the *in vivo* efficacy of a compound is not only determined by the affinity or activity of the compound on its target receptor in a validated *in vitro* assay, but by a range of other factors including the bioavailability of the compound, its pharmacokinetic profile, and the specificity of the compound for the desired target versus other potential targets.

*The amount of direction provided, the presence of working examples, and the quantity of experimentation necessary*

In the instant case, Interleukin-1 $\beta$  Microglial Cell Assay, Mouse Ear Inflammatory Response to Topical Arachidonic Acid, Skin Protection Assay, and E-Selectin Cell Inflammation Assays were performed in Examples 41-45. However, the skilled artisan would recognize and appreciate that an *in vitro* assay cannot duplicate the complex conditions of *in vivo* therapy. In the *in vitro* assay, the agent is in contact with cells during the entire exposure period. This is not the case *in vivo* where exposure to the target site may be delayed or inadequate. In addition, variables such as biological

stability, half-life, or clearance from the blood are important parameters in achieving successful therapy. The composition may be inactivated *in vivo* before producing sufficient effect. In addition, the composition may not reach its target because of its inability to penetrate tissues or cells. While the specification does contain statements regarding the use of the invention to treat dermatologic conditions in human subjects, the specification fails to enable such use. The specification fails to provide evidence that *in vitro* anti-inflammatory activity would reasonably correlate to successful methods of treating any dermatologic condition, such as those listed above, *in vivo*. One is left with speculation and an invitation to experiment. For the reasons discussed above, it would require undue experimentation for one skilled in the art to use the claimed methods. Therefore, the claimed invention lacks an enabling disclosure.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

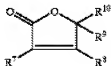
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The following reference, drawn to non-elected species, was found in the Information Disclosure Statement filed 11/25/2003. It should not be interpreted that a comprehensive search was performed for all non-elected species.

Claims 1, 5, 6, 8 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schulze zur Weische *et al.* (US 2003/0206933).

Schulze zur Weische discloses cosmetic agents comprising 2-furanone derivatives for the treatment of skin and hair (abstract). There is a need for active agents characterized by a reduction in undesired damage to skin and hair, and it has been found that derivatives of 2-furanone as active ingredient in cosmetic agents leads to surprisingly good properties of treated skin and hair (paragraph 0008). Damage to skin includes UV light (paragraph 0003), stressed skin, rough and irritable skin, etc. (paragraphs 0004-0007). Active agent can be used in combination with vitamins (paragraph 0216). Active agent is applied to the skin, such as in formulation including creams, lotions, emulsion, gels, etc. (paragraph 0271). Active cosmetic agents include 2-furanone derivatives of formula II (see claim 1):



Such compounds read on the instant claims, for example, when  $R^7$  is OH,  $R^8$  is  $NR^{12}R^{13}$ ,  $R^9$  is  $COOR^{14}$ ,  $R^{10}$  is either  $NR^{12}R^{13}$  or  $C_2-C_4$  hydrocarbon.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to use compounds having the claimed structure for use in treating a dermatologic condition. While *Schulze zur Weische* does not specifically exemplify a compound having the claimed structure for use in the claimed methods, given the general teaching of *Schulze zur Weische* that compounds having overlapping structural features as those claimed are useful in treating skin conditions, one of ordinary skill in the art at the time of the instant invention would have a reasonable expectation of success in formulating compounds according to *Schulze zur Weische* such that  $R^7$  is OH,  $R^8$  is  $NR^{12}R^{13}$ ,  $R^9$  is  $COOR^{14}$ ,  $R^{10}$  is either  $NR^{12}R^{13}$  or  $C_2-C_4$  saturated or mono or di-unsaturated, branched or linear hydrocarbon variables to be useful. Such compounds correspond to variables of the instant claims such that in Formula I,  $R^1$  is COOR,  $R^2$  is optionally substituted alkyl,  $R^3$  is optionally substituted alkyl,  $R^4$  is hydrogen, X is either lower alkylene or  $N(R')$ , Y is  $N(R')$ ,  $R'$  is hydrogen or alkenyl or optionally substituted alkyl, and also various instances of Formula III. A prima facie case of obviousness may be made when chemical compounds have very close structural similarities and similar utilities. "An obviousness rejection based on similarity in chemical structure and function entails the motivation of one skilled in the art to make a claimed compound, in the expectation that compounds similar in structure will have similar properties." *In re Payne*, 606 F.2d 303, 313, 203 USPQ 245, 254 (CCPA 1979). See *In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963) and *In re Dillon*, 919

F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1991). See also MPEP § 2144.08, paragraph II.A.4.(c).

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-10 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over the claims of U.S. Patent No. 6,667,330, in view of US 6,653,346.

The instant claims are drawn to a method of treating a dermatologic condition comprising administering a therapeutically effective amount of a compound of formula 1. Dependent claim 5 indicates that dermatologic conditions include regulating skin condition, regulating the signs of aging, treating dermatitis, skin irritation, acne, rosacea,

psoriasis, age-related disease, damage from UV radiation, among others. The claims of the '330 patent are drawn to methods of treatment for a mammal suffering from a condition characterized by oxidative stress, comprising administering an effective amount of a compound of claim 1. While the claims of the '330 patent do not specifically recite that a condition characterized by oxidative stress includes dermatologic conditions, including dermatitis, acne, psoriasis, rosacea, UV damage, etc., it is known in the art that the claimed dermatologic conditions are conditions characterized by oxidative stress, as evidenced by the claims of US 6,653,346. For example, see claims 18-22 of the '346 patent. Accordingly, the claims are overlapping in scope and are obvious variants of each other.

### ***Conclusion***

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is (571)272-9928. The examiner can normally be reached on Monday - Friday 8 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/  
Supervisory Patent Examiner, Art Unit 1618

LHS